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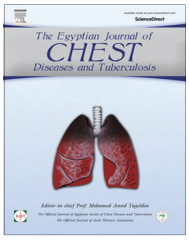

ORIGINAL ARTICLE

Pattern of hospital-acquired pneumonia in Intensive Care Unit of Suez Canal University Hospital

Mohamed Eida [a], **Mohamed Nasser** [b], **Nermine El-Maraghy** [c,*], **Khaled Azab** [a]

[a] *Endemic and Infectious Diseases, Faculty of Medicine, Suez Canal University, Egypt*
[b] *Chest Diseases, Faculty of Medicine, Suez Canal University, Egypt*
[c] *Medical Microbiology & Immunology, Faculty of Medicine, Suez Canal University, Egypt*

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KEYWORDS

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Abstract *Background:* Hospital acquired pneumonia occurs more than 48 h after hospital admission and was not present at the time of admission, while ventilator associated pneumonia occurs after 48–72 h of endotracheal intubation or within 48 h of extubation. HAP is the second most common nosocomial infection and accounts for approximately 25% of all infections in the Intensive Care Unit worldwide.

Purposes: To identify the etiology, initial evaluation, prevention, and treatment of adult patients with ICU HAP, and VAP in Suez Canal University hospital and their management strategies.

Methods: This study was conducted in the department of ICU, Suez Canal University Hospital; Ismailia, Egypt in the period from May to August 2013. All the patients were subjected to clinical and radiological assessment, Endotracheal aspirate samples for culture, and sensitivity to determine the causative organisms, Clinical Pulmonary Infection Score was done in order to determine the severity of HAP.

Results: 89% of patients were suffering from VAP, while 11% were suffering from HAP, with mean age of 63.8 ± 10.47 years. Methicillin-resistant *Staphylococcus aureus*, and *Klebsiella pneumoniae* represented the most common isolated organisms that accounted about 65% of the studied population. The isolated microorganisms were resistant to Amoxicillin, MRSA showed highest sensitivity (44.4%) to Vancomycin and (27.8%) to Imipenem. *K. pneumoniae* were sensitive mainly to Imipenem (75.9%) and to Levofloxacin (44.8%).

Conclusion: Gram-negative organisms were isolated in 46% of cases, gram-positive organisms in 41% and the isolated organisms showed high resistance to most of the tested antibiotics.

* Corresponding author at: Microbiology & Immunology Department, Faculty of Medicine, Suez Canal University, P.O. Box 536, 41111, Ring Road, Ismailia, Egypt. Tel./fax: +20 643356539; Cellphone: +20 124117033.
E-mail address: nermine76@hotmail.com (N. El-Maraghy).

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Introduction

Hospital-acquired pneumonia (HAP) is considered one of the most common nosocomial infections which accounts for approximately 25% of all infections in the intensive care unit (ICU) [1].

The difference between HAP and community acquired pneumonia (CAP) is the susceptibility of patients with HAP to pneumonia from different and potentially virulent pathogens [2].

While, HAP is closely related to ventilator-associated pneumonia (VAP) that refers to pneumonia that arises more than 48–72 h after endotracheal intubation, and the cause of infection is multidrug-resistant (MDR) bacteria [3].

There are many risk factors associated with HAP, and VAP and the presence of environmental and pharmacological factors [4].

The diagnosis of HAP is mainly diagnosed clinical through the endotracheal aspirate (ETA) cultures, white blood cell (WBC) count, serial chest radiographs, and arterial blood gases (ABG) [5].

The treatment of HAP started with broad-spectrum empiric antibiotics; then shifted to narrow-spectrum specific therapy to minimize the risk of resistance and adverse drug reactions over the treatment period, guided by microbiological results due to that the precise pathogen of HAP is usually unknown [6]. So, each ICU should design its own scheme for treatment on the basis of their microbiological results which has a major impact on patients' morbidity, mortality, and the economic aspect of their treatment [7].

We therefore aimed to identify the etiology, initial evaluation, prevention, and treatment of adult patients with ICU HAP, and VAP in Suez Canal University hospital (SCU) as well as the proper management strategies of patients with ICU HAP, and VAP.

Patients & methods

Patients

This study was conducted on 100 patients admitted to the department of ICU, SCU Hospital; Ismailia, Egypt who developed HAP or VAP during the period from May 2013 to October 2013 with an inclusion criteria of age range from 18 to 81 years old, of both sexes, showing symptoms & signs of pneumonia (productive cough with purulent sputum, and fever $\geqslant$38 °C, or hypothermia $\leqslant$36.3 °C).

With chest radiography showing newly developed signs of pneumonia (opacity of one lung segmental lobe, or bilateral opacities primarily in the bases of the lungs). HAP occurs more than 48 h after hospital admission, but was not present at the time of admission. VAP occurs after 48–72 h of endotracheal intubation.

We excluded patients with lung tumor, trauma, collapse, heart failure, pulmonary edema, patients with no radiographic shadows suggestive of pneumonia and or Neonates/pediatrics patients.

Methods

All patients were subjected to full history taking, clinical examination, laboratory investigations in the form of Complete blood count (CBC), arterial Blood Gases (ABG) {Roche OMNI C blood gases machine, made in Japan for Siemens Medical System, Inc, Issaquah, WA98029-7002USA}, Endotracheal aspirate (ETA) in order to make culture and sensitivity to determine the causative organisms.

All specimens were inoculated onto Blood agar, MacConkey agar, Mannitol salt agar, Chocolate agar, and Muller Hinton agar, incubated at 37 °C for 24 h. Gram stain and susceptibility test were performed to all specimens in order to diagnose the causative organism. Bacterial growth in these specimens is then quantitated and defined by the presence of bacteria above the predetermined threshold concentration (BAL $>10^4$ colony forming units [CFU]/ml). Plain posteroanterior and/or anteroposterior chest X-ray was performed to confirm the diagnosis, that showed newly developed evidence of pneumonia (opacity of one lung segmental lobe, or bilateral opacities primarily in the bases of the lungs).

The protocol of empiric antibiotic treatment employed in the SCU hospital before the culture results is to give Ceftazidime 1 g twice daily, plus Ampicillin/Sulbactam 1.5 g 3 times a day was given to 79% of the patients on admission to cover the most vulnerable gram positive, and gram negative microorganisms.

The Severity of HAP & VAP was assessed using Modified Clinical Pulmonary Infection Score (CPIS) [8] (Table 1).

Patients should have their CPIS recalculated daily, if the CPIS is less than 6, infection is unlikely and the decision to treat with antibiotics should be carefully considered.

Statistical analysis

Values are shown throughout the manuscript as number and percent as well as mean and standard deviation (SD). Results were compared using the Student *t*-test. A *P*-value equal or less than 0.05 was considered significant in all statistical tests. Statistical analyses and data blotting were performed using Microsoft excel by Microsoft Inc. and SPSS (SPSS 20.0 by SPSS software Inc.).

Table 1 Modified Clinical Pulmonary Infection Score (CPIS) chart.

Diagnostic feature	CPIS points		
	0	1	2
Tracheal secretions	Rare	Abundant	Abundant and purulent
Chest radiograph infiltrate	None	Diffuse	Localized
Temperature (°C)	$\geqslant$36.5 and $\leqslant$38.4	$\geqslant$38.5 and $\leqslant$38.9	$\geqslant$39 or $\leqslant$36
White blood cells ($\times10^9$/L)	$\geqslant$4.0 or $\leqslant$11.0	$<$4.0 or $>$11.0	$<$4.0 or $>$11.0 plus band forms $\geqslant$0.5
PaO_2/FiO_2 mmHg	$>$240 or ARDS		$\leqslant$240 and no ARDS
Microbiology	Negative	Positive	Positive plus positive Gram stain

Ethical considerations

The study work got approval from the Ethics Committee of Faculty of Medicine, Suez Canal University (FOMSCU); Ismailia, Egypt.

Table 2 Demographic data of the studied patients.

Specification		Freq. (n = 100)	%
Age	⩽65 years	77	77
	>65 years	23	23
Sex	Male	73	73
	Female	27	27

Results

Results are mentioned in Tables 2–10.

Discussion

This study was conducted on 100 cases admitted to the department of ICU, SCU Hospital; Ismailia, Egypt who developed HAP or VAP during the period from May to October 2013, to investigate the etiology, prevention, initial evaluation, and treatment in order to identify the proper management strategies of these patients. The mean age of the patients was 63.8 ± 10.47 years with an range from 18 to 81 years, this was comparable to the mean age of the patients included in a study conducted by Holzapfel et al. [9] who recognized that

Table 3 Clinical data of the studied patients.

Specification		Freq. (n = 100)	%
Concomitant illness	Diabetes mellitus (DM)	4	4
	Hypertension	9	9
	Ischemic heart disease (IHD)	3	3
	Chronic obstructive pulmonary disease (COPD)	4	4
	DM + Hypertension	24	24
	DM + Hypertension + IHD	11	11
	DM + IHD + COPD	2	2
	Hypertension + COPD	1	1
	OTHERS	11	11
	NONE	31	31
Cause of ICU admission	Acute myocardial infarction	3	3
	Cor pulmonale	4	4
	Acute respiratory distress syndrome (ARDS)	10	10
	Motor car accident	24	24
	Decompensated heart failure	5	5
	Cerebrovascular accident	21	21
	OTHERS	32	32
Onset of pneumonia	Early (⩽4 days)	17	17
	Late (>4 days)	83	83
Severity of pneumonia	Mild	18	18
	Moderate	47	37
	Severe	35	35
Antibiotics given on admission	Cefipime	7	7
	Ceftazidime	2	2
	Levofloxacin	3	3
	Cefoperazone + Amp/Sulb	2	2
	Ceftazidime + Ampicillin/Sulb	79	79
	Levofloxacin + Imipenem	1	1
	Cefipime + Amp/Sulb	1	1
	Levofloxacin + Clindamycin	1	1
	Ceftazidime + Cefipime	1	1
	Ceftriaxone + Levofloxacin	1	1
	Meropenem + Clindamycin	1	1
	Cipro + Erythromycin + Cefipime	1	1
Smoking	Smokers	48	48
	Non smokers	52	52
Mechanical ventilation	Ventilated	89	89
	Non ventilated	11	11
Fate of the patients	Discharged	37	37
	Died	63	63

Table 4 The relation between the isolated organisms and the mechanical ventilation.

Isolated organisms	Total No.	Mechanical ventilation (n = 100)			
		Ventilated (VAP)		Non ventilated (HAP)	
		Freq.	% of column	Freq.	% of column
Methicillin resistant *Staph.aureus* (MRSA)	36	32	35.9	4	36.35
Klebsiella pneumoniae	29	25	28.1	4	36.35
Pseudomonas aeruginosa	6	5	5.7	1	9.1
Proteus spp.	6	6	6.8	0	0.0
E. coli	5	5	5.6	0	0.0
Strept. viridans	3	2	2.2	1	9.1
Methicillin sensitive *Staph.aureus* (MSSA)	2	2	2.2	0	0.0
No growth	13	12	13.5	1	9.1
Total	100	89	100	11	100

P value = 0.88.

Table 6 The relation between the detected organisms and the age.

Isolated organisms	Total No	Age			
		⩽65 years		>65 years	
		Freq.	% of column	Freq.	% of column
MRSA	36	30	39	6	26.3
Klebsiella pneumoniae	29	20	25.9	9	39.3
Pseudomonas aeruginosa	6	5	6.5	1	4.3
Proteus spp.	6	5	6.5	1	4.3
E. coli	5	4	5.1	1	4.3
Strept. viridans	3	1	1.3	2	8.6
Methicillin sensitive *Staph.aureus* (MSSA)	2	2	2.6	0	0.0
No growth	13	10	13.1	3	12.9
Total	100	77	100.0	23	23.0

P value = 0.29.

pneumonia is more likely to develop in the elderly period and paid attention to the rising rate of mortality from pneumonia with extreme of ages.

The main obstacles we faced in this study are the limited number of available ICU beds, prolonged patient admission time due to their primary illness, and the superadded admission time due to their HAP. Also, the inability to culture important causative microorganisms such as *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*, as well as fungal and viral microorganisms due to financial shortage, and difficulty of the procedures.

For the microbiological results of the VAP group, we found that 35.9% of patients were infected by MRSA, followed by *Klebsiella pneumoniae* (28.1%), Proteus species (6.8%), *Pseudomonas aeruginosa* (5.7%), *Escherichia coli* (5.6%), *Streptococcus viridans* (2.2%), and Methicillin sensitive *Staph.aureus* (MSSA) (2.2%) (Table 4). Mechanical ventilation is associated with high rates of HAP because the endotracheal tube bypasses upper respiratory tract defenses, allows for pooling of oropharyngeal secretions, prevents effective cough, and infection. Likely Samah et al. [12] studied HAP in the ICU of Police Hospitals and found that the most common isolated organisms were MRSA (22%) followed by *Acinetobacter species* (20%), *K. pneumoniae* (18%), *P. aeruginosa* (15%).

While in the non-ventilated HAP group, the results revealed that MRSA, and *K. pneumoniae* are equally isolated (36.35%), followed by *P. aeruginosa* (9.1%), and *Streptococcus viridans* (9.1%) (Table 4). El Solh et al. [10] study agreed with our results in that the most frequent causes of HAP were MRSA (33%), gram-negative enteric bacilli (24%), and Pseudomonas species (14%).

Our research showed partial agreement with the study conducted by Queenan et al. [11] which revealed that *Pseudomonas aeruginosa* and *Klebsiella* species were the most prevalent organisms in the pathogenesis of HAP, and together they accounted for approximately half of all organisms. Also we found partially agreement with the results of Maha et al. [13] who studied the diagnostic value of BAL in VAP of pediatric patients, and Hassan et al. [14].

Table 5 The relation between the detected organisms and the severity of pneumonia.

Isolated organisms	Total No.	Severity of pneumonia (n = 100)					
		Mild		Moderate		Severe	
		Freq.	% of column	Freq.	% of column	Freq.	% of column
MRSA	36	2	11.1	18	38.3	16	45.7
Klebsiella pneumoniae	29	6	33.3	17	36.2	6	17.1
Pseudomonas aeruginosa	6	1	5.6	1	2.1	4	11.4
Proteus spp.	6	4	22.2	1	2.1	1	2.9
E. coli	5	3	16.7	0	0.0	2	5.8
Strept. viridians	3	0	0.0	3	6.4	0	0.0
Methicillin sensitive *Staph.aureus* (MSSA)	2	0	0.0	2	4.2	0	0.0
No growth	13	2	11.1	5	10.8	6	17.1
Total	100	18	100.0	47	100.0	35	100.0

P value = 0.007.

The significantly high rate of gram-negative bacilli in our work and many other studies probably indicates the high incidence of prolonged hospital stay and the prolonged duration of mechanical ventilation that predisposes the patients to acquire infections from the MDR pathogens.

Magdy et al. [15] studied HAP in five major Egyptian Military Hospitals (Kobbry El kobba, El-Maadi, Masr Elgadida, El-Galaa and Ghamra) and reported that gram negative organisms were the most prevalent in HAP especially *K. pneumoniae* (23.1%), followed by *P. aeruginosa* (17.3%), and *E. coli* (11.5%), while *Staphylococcus haemolyticus* (7.7%) was the most prevalent gram positive organism.

Patra et al. [16] reported that VAP constituted 76% of patients with HAP and represented the most frequent nosocomial infection in the ICU (80%), with an overall mortality of HAP reaching 60%; all were secondary to gram-negative infections with *P. aeruginosa* contributing to 57.1% of deaths followed by *K. pneumoniae*, *E. coli* and Acinetobacter species. The increasing incidence of infections caused by MDR pathogens contributes to the emerging seriousness of these infections with expected higher mortality rate.

In contrast, other authors reported other bacterial strains. Amal et al. [17] who studied 160 patients having pneumonia in both Cairo and Tanta University Hospitals, of which only 7.5% of them having HAP, found that two major organisms were responsible for HAP; namely *Streptococcus pneumoniae* and *K. pneumoniae*; 33.3% for each, followed by *Hemophilus influenzae* and *Streptococcus pyogenes*; 11.1% for each, this difference may be due to the small number of patients with HAP in their study.

Also unlikely to this study, Nadia et al. [18] were studying the atypical bacteria in the ICU of Critical Care Department in the Alexandria Main University Hospital, and found that Candida species was the commonest isolated organism accounting for 23.3%, followed by *P. aeruginosa* (21.6%), then the polymicrobial growth (20%), *Staphylococcus aureus* (16%), Acinetobacter species (8.3%), Proteus species 6.6%, Klebsiella species (6.6%), *E. coli* (5%), Coagulase-negative staphylococci (1.6%), and Diphtheroids (1.6%). It is also to be noted that 31.6% of the total ETA of the 60 VAP cases were negative by the conventional microbiological culture.

Antibiotic therapy and critical illness can suppress the normal bacterial flora and lead to an over-growth of Enterobacteriaceae like *K. pneumoniae* in the respiratory tract. The most concerning is the acquisition of ESBL that render the bacteria resistant to penicillin and cephalosporin antibiotics, and may cause serious nosocomial infections especially in critically ill patients. Laurent et al. [19] have described numerous outbreaks with ICU-acquired ESBL-producing *K. pneumoniae*, where infection increased from a baseline rate of 0.44 cases per 1000 patient days to 6.86 cases per 1000 patient-days.

We found that about 13% of ETA showed that no growth on routine culture, so polymerase chain reaction (PCR) reaction is recommended for these cases in the future studies according to the finding of Nadia et al. [18] that found positive PCR results for atypical bacteria in 9 (15%) out of 60 samples, 5 were positive for *M. pneumoniae*, 3 for *L. pneumophila*, and only 1 was positive for *C. pneumoniae*, and concluded that atypical bacteria are not an uncommon cause for HAP, and VAP.

Table 7 The relation between concomitant illness and the severity of pneumonia (N = 100).

Concomitant illness	Total No.	Severity of pneumonia					
		Mild		Moderate		Severe	
		Freq.	% of column	Freq.	% of column	Freq.	% of column
DM	41	2	11.1	23	48.9	18	51.4
COPD	7	3	16.7	3	6.4	1	2.9
OTHERS	21	3	16.7	10	21.3	7	20.0
NONE	31	10	55.5	11	23.4	9	25.7
Total	100	18	100.0	47	100.0	35	100.0

P value = 0.04.

Table 8 The relation between the isolated organisms and the sensitivity to the tested antibiotics.

Isolated organisms	Tested antibiotic						
	Vancomycin (%)	Imipenem (%)	Levofloxacin (%)	Ceftriaxone (%)	Cefoperazone (%)	Cefotaxime (%)	Amoxicillin (%)
MRSA	44.4	27.8	11.1	8.3	19.4	8.3	0
Klebsiella spp.	3.4	75.9	44.8	13.8	3.4	0	0
P. aeruginosa	66.7	50	66.7	0	0	0	0
Proteus spp.	50	16.7	33.3	83.3	16.7	33.3	0
E. coli	0	80	40	20	20	0	0
Strept. Viridians	0	66.7	33.3	33.3	0	0	0
Methicillin sensitive *Staph.aureus* (MSSA)	0	0	0	0	0	0	0

P value = 0.32.

Compared to the study conducted by Ibrahim et al. [20] who studied the microbiology of HAP in elderly patients in a community hospital in the Pulmonary and Critical Care Medicine Division at Washington University, School of Medicine found that in early onset HAP, the so called main pathogens include community pathogens such as MSSA, *S. pneumoniae* and *H. influenzae* as well as gram-negative enteric bacilli are predominate. While in late onset HAP; MRSA, *P. aeruginosa* and *K. pneumoniae* are frequently encountered.

On the other hand, in this study 24% of enrolled patients with HAP were admitted primarily to the ICU due to MCA, followed by 21% due to CVA, compared to Ibrahim et al. [20] study who conducted a comparative analysis of patients with early-onset versus late-onset ICU HAP, and found the primary cause of admission is IHD (32.1%), followed by CVA (24.2%), then ARDS (19.2%).

Severe concomitant illness predisposes patients in the ICU to the development of HAP, and contributes to the associated high mortality rates, as in this study more than third of the patients had pre-existing illnesses, with DM being the most common, and the combination of DM and hypertension in 24% of patients (Table 7), that agrees with El Solh et al. [10] study that found that 72% had at least the same two concomitant illnesses, while 23% had 3 or more concomitant illnesses.

Resistance to antibiotics is rapidly evolving. In this study, the isolated microorganisms are totally resistant to Amoxicillin. MRSA showed highest sensitivity (44.4%) to Vancomycin, then (27.8%) to Imipenem, while it was almost resistant to all other tested antibiotics. *K. pneumoniae* were sensitive mainly to Imipenem (75.9%), then to Levofloxacin (44.8%), and also almost resistant to all other tested antibiotics (Table 8). This was in agreement with Gamal Agmy et al. [21] who conducted their study in Upper Egypt and found that the causative organisms of HAP were MRSA (23%), K. pneumoniae (14%), and polymicrobial (12%). A higher sensitivity was recorded for vancomycin, ciprofloxacin, and moxifloxacin. Very high resistance was recorded for β-lactam-β-lactamase inhibitors and cephalosporins.

In our research, the mortality rate was 63%, mortality associated with HAP due to MRSA was 47.7%, and 26.9% for HAP due to *K. pneumoniae*, followed by 7.9% in HAP due to *P. aeruginosa* (Table 10).

The prognosis for HAP caused by gram-negative bacilli is worse than HAP caused by gram-positive pathogens, death rates associated with *P. aeruginosa* are particularly high, ranging from 70% to more than 80% in several studies, according to Garnacho-Montero et al. [22] who found that the mortality associated with *P. aeruginosa* or *Acinetobacter pneumonia* was 87% compared with 55% for pneumonias due to other organisms. While in cases caused by gram-positive pathogens, comparing VAP due to MRSA or MSSA, mortality was found to be directly attributable to pneumonia for 86% of the former causes versus 12% of the latter, with a relative risk of death equal to 20.7 for MRSA pneumonia.

Also Chawla [23] admitted higher frequencies of mortalities associated with MRSA, Enterobacter species, and *P. aeruginosa*, in a 6-year surveillance study from the period 2002 to 2007 involving ICUs in Latin America, Asia, Africa, and Europe, using the CDC National Nosocomial Infections Surveillance (NNIS) definitions, also reported higher rates of HAP, and VAP than those of comparable United States ICUs.

Table 9 The relation between used antibiotics before ICU admission, and the isolated organisms ($N = 29$).

Used antibiotic	Number	%	Isolated organism
Ceftriaxone	3	21.4%	MRSA
Cefotaxime	3	21.4%	MRSA
Levofloxacin	3	21.4%	*Klebsiella* spp.
Ciprofloxacin	2	14.4%	MRSA
Azithromycin	3	21.4%	MRSA
Total	14	100%	
Unknown antibiotics	15	46.7%	MRSA
		40%	*Klebsiella* spp.
		13.3%	*P. aeruginosa*
Total	15	100%	

Table 10 Relation between causative organisms and fate of the patients.

Isolated organisms	No.	Fate ($n = 100$)			
		Discharged		Died	
		Freq.	% of column	Freq.	% of column
MRSA	36	6	16.2	30	47.7
Klebsiella pneumoniae	29	12	32.4	17	26.9
P. aeruginosa	6	1	2.7	5	7.9
Proteus spp.	6	5	13.5	1	1.6
E. coli	5	4	10.9	1	1.6
Strept. viridans	3	2	5.4	1	1.6
Methicillin sensitive *Staph.aureus* (MSSA)	2	2	5.4	0	0
No growth	13	5	13.5	8	12.7
Total	100	37	100	63	100

P value = 0.004.

Conclusion

The Gram-negative organisms were isolated in 46% of cases, gram-positive organisms were isolated in 41% and the isolated organisms showed high resistance to most of the tested antibiotics.

Competing interests

The authors declare that they have no competing interests.

Author's contribution

All authors participated in the design of the study. Kaled Azab has provided the patients and reviewed the manuscript. Mohamed Eida, Mohamed Nasser and Nermine El-Maraghy designed the study, carried out clinical and the laboratory work, wrote and edited the manuscript. All authors read and approved the final manuscript.

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References

[1] L. Dunn, Pneumonia: classification, diagnosis and nursing management, J. Nurs. Stand. 19 (42) (2005) 50–54, 5.
[2] American Thoracic Society; Infectious Diseases Society of America, Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia, Am. J. Respir. Crit. Care Med. 171 (2005) 388–416.
[3] B.A. Cunha, Multi-drug resistant (MDR) *Klebsiella*, *Acinetobacter*, and *Pseudomonas aeruginosa*, Antibiot. Clin. 10 (2008) 354–355.
[4] M.H. Kollef, The prevention of ventilator-associated pneumonia, N. Engl. J. Med. 340 (2009) 627–634.
[5] J.H. Bates, S. Wagers, L. Lundblad, et al, Nonlinearity of respiratory mechanics during bronchoconstriction in mice with airway inflammation, J. Appl. Physiol. 92 (5) (2002) 1802–1807.
[6] G.J. Noel, R. Strauss, A. Shah, et al. Ceftobiprole Versus Ceftazidime Combined with Linezolid for Treatment of Patients with Nosocomial Pneumonia, Program and abstracts of the 48th Annual ICAAC, IDSA 46th Annual Meeting, Washington, DC, 2008.
[7] Z. Hoare, Pneumonia: update on diagnosis and management, BMJ 6 (332(7549)) (2006) 1077–1079.
[8] M. Fartoukh, B. Maitre, S. Honoré, et al, Diagnosing pneumonia during mechanical ventilation: the clinical pulmonary infection score revisited, Am. J. Respir. Crit. Care Med. 168 (2003) 173–179.
[9] L. Holzapfel, L. Biot, G. Becq, et al, Do we need a systematic activation of alarm soundings for blood pressure monitoring for the safety of ICU patients?, J Crit. Care 18 (4) (2003) 212–216.
[10] A.A. El Solh, A.T. Aquilina, R.S. Dhillon, et al, Impact of invasive strategy on management of antimicrobial treatment failure in institutionalized older people with severe pneumonia, Am. J. Respir. Crit. Care Med. 166 (2002) 1038–1043.
[11] A.M. Queenan, B. Foleno, C. Gownley, et al, Effects of inoculum and beta-lactamase activity in AmpC- and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* clinical isolates tested by using NCCLS ESBL methodology, J. Clin. Microbiol. 42 (1) (2004) 269–275.
[12] M.E. Samah, Pathogens causing ICU Acquired Pneumonia in Police Hospitals, Master Degree in Chest Disease, Faculty of Medicine, Ain Shams University, 2006.
[13] M. Maha, A. Fatma, E. Tharwat, Diagnostic value of bronchoalveolar lavage in ventilator associated pneumonia of pediatric patients, Egypt. J. Med. Lab. Sci. 17 (1) (2008) 11–25.
[14] A. Hassan, A. Samy, K. Bedewy, VAP: the role of typical bacteria and atypical bacteria and Fungi. Comparison between endotracheal aspirates and bronchoalveolar lavage, EJB 1 (1) (2007) 53–61, 1.
[15] Magdy M. Khalil, Aya M. Abdel, Ayman Abd. Dayem, Al.-Hameed. Farghaly, et al, Pattern of community and hospital acquired pneumonia in Egyptian military hospitals, Egypt. J. Chest Dis. Tuberc. 62 (2013) 9–16.
[16] P.K. Patra, M. Jayashree, S. Singhi, et al, Nosocomial pneumonia in a pediatric intensive care unit, J. Indian Pediatr. 44 (2007) 511–518.
[17] Amal A. Wafy, Kamal M. Hanna, Ayman. Salem, et al, A study on the aetiology of pneumonia in Cairo and Tanta University Hospitals: a bacteriologic approach, Egypt. J. Med. Microbiol. 17 (1) (2008) 57–65.
[18] Nadia A. Mokhless, Malaka F. El-Mofty, Nesrine F. Hanafi, et al, Atypical bacteria in ventilator associated pneumonia; an Egyptian University Hospital experience, J. Am. Sci. 6 (12) (2010) 1074–1079.
[19] C. Laurent, H. Rodriguez-Villalobos, F. Rost, et al, Intensive care unit outbreak of extended spectrum β-lactamase-producing *Klebsiella pneumoniae* controlled by cohorting patients and reinforcing infection control measures, J. Infect. Control. Hosp. Epidemiol. 29 (2008) 517–552.
[20] E.H. Ibrahim, S. Ward, G. Sherman, A comparative analysis of patients with early-onset vs late-onset nosocomial pneumonia in the ICU setting, J. Chest 117 (2000) 1434–1442.
[21] Gamal. Agmy, Sherif. Mohamed, Yaser. Gad, Esam. Farghally, Hamdy. Mohammedin, Hebba. Rashed, Bacterial profile, antibiotic sensitivity and resistance of lower respiratory tract infections in upper Egypt, J. Mediterr. J. Hematol. Infect. Dis. 5 (1) (2013) e2013056.
[22] J. Garnacho-Montero, C. Ortiz-Leyba, F.J. Jiménez-Jiménez, et al, Treatment of multidrug-resistant *Acinetobacter baumannii* ventilator-associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP, J. Clin. Infect. Dis. 36 (9) (2003) 1111–1118.
[23] R. Chawla, Epidemiology, etiology, and diagnosis of hospital acquired pneumonia and ventilator-associated pneumonia in Asian countries, J. Am. J. Infect. Control. 36 (4) (2008) S93–S100.